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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/822,295	04/02/2001	Bahija Jallal	038602/1125	8862

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EXAMINER
HOLLERAN, ANNE L

ART UNIT	PAPER NUMBER
1642	13

DATE MAILED: 07/15/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/822,295	JALLAL ET AL.	
	Examiner	Art Unit	
	Anne Holleran	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 April 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *12 and 23-34* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *12 and 23-34* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a)☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1)☐ Notice of References Cited (PTO-892)
2)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3)☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4)☐ Interview Summary (PTO-413) Paper No(s). _____ .
5)☐ Notice of Informal Patent Application (PTO-152)
6)☐ Other:

DETAILED ACTION

1. The amendment filed April 4, 2003 is acknowledged. Claims 10 and 11 were canceled. Claims 23-34 were added. Claims 12 and 23-34 are pending and examined on the merits.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections Maintained and New Grounds of Rejection:

3. Claims 12, 23-31, 33 and 34 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. New grounds of rejection are presented.

Claim 12 is indefinite because it is drawn to polypeptides that comprise an amino acid sequence that is at least 90% identical to the entire sequence of SEQ ID NO: 2, but also lacks amino acid residues 1-48, 49-294 or 295-807 (or N-terminal domain, catalytic domain, or C-terminal domain). Since SEQ ID NO: 2 is 807 amino acids in length, the most that the claimed protein could lack, and still have 90% identity to the entire amino acid sequence of SEQ ID NO: 2, would be 80 amino acids. Thus, the claim does not make sense to the extent that it has 90 percent identity to SEQ ID NO: 2 and lacks either portion amino acids 49-294 or lacks portion amino acids 295-807.

Claim 34 is also indefinite because it lacks antecedent basis for "said non-PTP-04 polypeptide".

4. Claims 12 and new claims 23, 25-34 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for polypeptides that comprise the amino acid sequence set forth in SEQ ID NO: 2, does not reasonably provide enablement for the full scope of the claimed genus of PTP04 polypeptides, as contemplated in the specification, page 16, line 24 to page 22, line 23, and as claimed in claims 12 or 32, where the claimed polypeptides may only comprise a fragment of SEQ ID NO: 2; or as claimed where the polypeptide comprises a sequence that has either 90 or 95% identity to SEQ ID NO: 2, or to a portion of SEQ ID NO: 2. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Applicant's arguments have been carefully considered, but are not persuasive. Applicant argues that one of skill in the art would be able to use the claimed polypeptides as a phosphatase enzyme, in a truncated form to find natural binding partners and for the purpose of making antibodies. However, as set forth in the previous Office action, the only use that is enabled by the specification is the use of those polypeptides that have phosphatase activity. The claims as currently recited are not limited to polypeptides that have phosphatase activity.

The claims are broadly drawn to isolated, enriched or purified PTP04 polypeptides, polypeptides comprising fragments of a protein encoded by the amino acid sequence of SEQ ID NO: 2, and drawn to polypeptides that lack one or more segments of the polypeptide of SEQ ID NO: 2, where the segments are defined as amino acid residues, 1-48, 49-294, 295-807, an N-

terminal domain, a catalytic domain, and a C-terminal domain. Thus, the claims are drawn to a large genus of polypeptide structures, where many of the species have very little in common with the structure of the one exemplified PTP04 polypeptide, that of a polypeptide having the amino acid sequence of SEQ ID NO: 2.

The specification teaches one example of a PTP04 polypeptide, and teaches that it is defined by the primary amino acid sequence set forth in SEQ ID NO: 2. This sequence is derived from a cDNA sequence that was discovered to be differentially expressed in tumor cells relative to non-tumor cells, and is asserted to be the sequence of an intracellular tyrosine phosphate. Therefore, the specification enables the use of polypeptides comprising the full sequence of SEQ ID NO: 2, because such a sequence has enzymatic activity of a tyrosine phosphatase, and may be used by one of skill in the art to catalyze a tyrosine phosphatase reaction. However, the specification fails to disclose any examples of variants of SEQ ID NO: 2 that could be used by one of skill in the art to catalyze a tyrosine phosphatase reaction. The description of PTP04 polypetpides that is provided in the specification amounts to a wish or hope of discovering variants that are encompassed by the claimed genus. Thus, although the specification provides a description of what structures are contemplated, this does not amount to an enabling disclosure for how to use the a representative number of species, because it is not clear that the described variants will have the same enzymatic activity, or any activity at all, that the polypeptide comprising the amino acid sequence of SEQ ID NO: 2 has.

Furthermore, the study of the relationship between the primary amino acid sequence and protein function is highly unpredictable. Bowie et al (Science, 247: 1306-1310, 1990) teaches that while it is known that many amino acid substitutions are possible in any given protein, the

position with the protein sequence where such amino acid substitutions can be made with a reasonable expectation of maintaining function are limited. Burgess et al (J. Cell Biology, 111 : 2129-2138, 1990) teaches that replacement of a single lysine residue at position 118 of acidic fibroblast growth factor by glutamic acid led to the substantial loss of heparin binding, receptor binding and biological activity of the protein. Lazar et al (Molecular and Cellular Biology, 8: 1247-1252, 1988) teaches that replacement of aspartic acid at position 47 with alanine or asparagines does not affect biological activity while replacement with serine or glutamic acid sharply reduces the biological activity of the protein. These references demonstrate that even a single amino acid substitution will often dramatically affect the biological activity and characteristics of a protein. Therefore, the claims are drawn to a highly variant genus of polypeptide structures, which may have widely varying biogical functions, or no function at all.

It is noted that the specification teaches that the mRNA that encodes the amino acid sequence of SEQ ID NO: 2 is differentially expressed in tumor cells. However, this teaching is not sufficient to enable one of skill in the art to use the encoded protein for diagnosis of cancer, because the relationship between cancer and the expression of the protein product is not established by the disclosure of the specification. Many other proteins are regulated at the translational level rather than the transcriptional level. For instance, Shantz and Pegg (Int J of Biochem and Cell Biol., 1999, Vol. 31, pp. 107-122) teach that ornithine decarboxylase is highly regulated in the cell at the level of translation and that translation of ornithine decarboxylase mRNA is dependent on the secondary structure of the mRNA and the availability of eIF-4E, which mediates translation initiation. McClean and Hill (Eur J of Cancer, 1993, vol. 29A, pp.2243-2248) teach that p-glycoprotein can be overexpressed in CHO cells following exposure

to radiation, without any concomitant overexpression of the p-glycoprotein mRNA. In addition, Fu et al (EMBO Journal, 1996, Vol. 15, pp. 4392-4401) teach that levels of p53 protein expression do not correlate with levels of p53 mRNA levels in blast cells taken from patients with acute myelogenous leukemia, said patients being without mutations in the p53 gene. Thus, predictability of protein translation is not necessarily contingent on mRNA expression due to the multitude of homeostatic factors affecting transcription and translation. Thus, given the state of the art as reviewed above, the differential expression of mRNA in tumor cells cannot be used as a basis for the proposition that detection of the claimed polypeptides may be used for detection of tumor cells, because the specification has not correlated the expression of the claimed polypeptides with the treatment or diagnosis of a disease.

Because the enablement of the one exemplified species of PTP04 is narrowly based on the ability of one of skill in the art to use the polypeptide as tyrosine phosphatase, the specification fails to enable the claims that are directed to polypeptides comprising fragments, or to polypeptides that are sequence variants of PTP04, because it is highly unpredictable whether any of these species will have the same biological activity as that of the exemplified polypeptide comprising the amino acid sequence of SEQ ID NO: 2. Therefore, in view of the broadly claimed genus, the narrow basis for the enablement of use of the exemplified polypeptide species and the unpredictable nature of protein chemistry, it would require undue experimentation for one of skill in the art to use polypeptides as claimed.

5. The rejection of claim 12 under 35 U.S.C. 102(a) as being anticipated by Accession No. Q93095, Database SPTREMBL, 01 February 1997, Dayton, M.A. et al) is maintained and

applied to new claims 27, and 29. Applicant's arguments have been carefully considered, but are unpersuasive. The rejection is maintained because claims 12, 27 and 29 are unclear in the recitation of having 90% or 95% identity to the full length of SEQ ID NO: 2, but also lacking a fragment that is greater than either 10 or 5% of SEQ ID NO: 2.

Claims 12, 27 and 29 may be interpreted as drawn to polypeptides that comprise fragments of SEQ ID NO: 2. Accession No. Q93095 teaches a polypeptide that comprises amino acids 164-243 of SEQ ID NO: 2, thus, describing a sequence that lacks at least one of the domains listed in claim 12. Therefore, Accession No. Q93095 teaches a polypeptide that is the same as that claimed.

6. The rejection of claims 12 under 35 U.S.C. 102(b) as being anticipated by Matthews et al (Matthews, R.J. et al., Mol. Cell. Biol. 12: 2396-2404, 1992; cited in the IDS) is maintained and applied to new claims 27 and 29. Applicant's arguments have been carefully considered, but are unpersuasive. The rejection is maintained because claims 12, 27 and 29 are unclear in the recitation of having 90% or 95% identity to the full length of SEQ ID NO: 2, but also lacking a fragment that is greater than either 10 or 5% of SEQ ID NO: 2.

Claims 12, 27 and 29 may be interpreted as drawn to polypeptides that comprise fragments of SEQ ID NO: 2. Matthews teaches a polypeptide sequence that comprises amino acids 89-120 of SEQ ID NO: 2, thus describing a sequence that lacks at least at least one of the domains listed in claim 12. Thus, Matthews teaches a polypeptide that is the same as that claimed.

7. The rejection of claims 12 under 35 U.S.C. 102(e) as being anticipated by Cheng et al (U.S. 6,238,902; issued May 29, 2001; effective filing date March 20, 1997) is maintained and applied to new claims 27, 29, 31, 33 and 34. Applicant's arguments have been carefully considered, but are unpersuasive. The rejection is maintained because claims 12, 27 and 29 are unclear in the recitation of having 90% or 95% identity to the full length of SEQ ID NO: 2, but also lacking a fragment that is greater than either 10 or 5% of SEQ ID NO: 2.

Claims 12 may be interpreted as drawn to polypeptides that comprise fragments of SEQ ID NO: 2 or that have high sequence similarity with the amino acid sequence of SEQ ID NO: 2 over a portion of SEQ ID NO: 2. Cheng teaches a polypeptide that comprises the fragment of SEQ ID NO: 2, amino acids 790-802, thus, describing a sequence that lacks at least one of the domains listed in claim 12. Also, Cheng teaches a polypeptide that has almost 90 percent sequence similarity over amino acids 24 to 294 of SEQ ID NO: 2. Cheng teaches GST fusion polypeptides (col. 31, lines 48-67) and pharmaceutical compositions (col. 21, lines 55-62). Thus, Cheng discloses a polypeptide sequence that is the same as that claimed.

Conclusion

No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the Office should be directed to Anne Holleran, Ph.D. whose telephone number is (703) 308-8892. Examiner Holleran can normally be reached Monday through Friday, 9:30 am to 2:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa, Ph.D. can be reached at (703) 308-3995.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist at telephone number (703) 308-0196.

Anne L. Holleran
Patent Examiner
July 14, 2003

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